REMARKS

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested. Pursuant to 37 CFR § 1.121, attached as Appendix A is a Version With Markings to Show Changes Made.

The rejection of claims 1-4 and 6-9 under 35 U.S.C. § 112 (2nd para.) for indefiniteness is respectfully traversed in view of the above amendments.

The rejection of claims 1-4, 6-9, 19-22, and 24-27 under 35 U.S.C. § 112 (1st para.) for lack of enablement is respectfully traversed.

The U.S. Patent and Trademark Office ("USPTO") has acknowledged that the specification is enabling for methods of identifying an ion channel blocker and of screening for a drug for effectiveness as an ion channel blocker, where the ion channel is a Kv1.2 channel. However, the USPTO believes that the specification is not enabling for such methods involving any other type of ion channel. Applicant respectfully disagrees. In support of its position, applicant submits herewith the Declaration of Xin-Yun Huang Under 37 CFR § 1.132 ("Huang Declaration").

As discussed below, the Huang Declaration demonstrates (1) that it is well recognized in the art that external vestibules of all potassium, calcium, and sodium channels have similar structures (Huang Declaration ¶ 4), and (2) that it has been demonstrated that inhibition of ion channel activity is due to binding of a blocking agent (e.g., an antibody) to a particular peptide sequence located in the external vestibule of an ion channel (Id.).

As stated in paragraph 5 of the Huang Declaration, as evidenced by various publications involving ion channel investigations, it is accepted in the relevant field of expertise that external vestibules of all potassium, calcium, and sodium channels have similar structures. See Doyle et al., "The Structure of the Potassium Channel: Molecular Basis of K^+ Conduction and Selectivity," Science 280:69-77 (1998) ("Doyle") (attached to the Huang Declaration as **Exhibit 1**); MacKinnon et al., "Structural Conservation in Prokaryotic and Eukaryotic Potassium Channels," Science 280:106-109 (1998) ("MacKinnon") (attached to the Huang Declaration as **Exhibit 2**); and Lu et al., "Ion Conduction Pore Is Conserved Among Potassium Channels," Nature 413:809-813 (2001) ("Lu") (attached to the Huang Declaration as **Exhibit 3**). Because of the structural similarity of the external vestibules of ion channels, it is not necessary to know which part of the ion channel constitutes the external vestibule in order to practice the methods of the present invention (Huang Declaration ¶ 5).

This is evidenced by the use of the claimed technology to inhibit a store-operated Ca^{2+} channel, as reported in Xu et al., "TrpC1 Is a Membrane-Spanning Subunit of Store-Operated Ca^{2+} Channels In Native Vascular Smooth Muscle Cells," Circulation Research 88:84-87 (2001) ("Xu") (attached to the Huang Declaration as **Exhibit 4**) (Huang Declaration ¶ 5).

Further, contrary to the USPTO's position, it is of no consequence that all ion channels do not have six transmembrane regions (Huang Declaration ¶ 6). Although most potassium channels do, indeed, have six transmembrane regions, even ion channels (including potassium channels) with less than six transmembrane regions have regions equivalent to the S5 and S6 regions (also referred to as M1 and M2 regions) as recited in the claims (Id.). See Jan et al., "Cloned Potassium Channels From Eukaryotes and Prokaryotes," Ann. Rev. Neurosci. 20:91-123 (1997) ("Jan") (attached to the Huang Declaration as **Exhibit 5**). Thus, one of ordinary skill in the art would be fully able to practice the methods of the present invention, as defined in the amended claims.

The USPTO has also taken the position that the methods of claims 1-3 and 6-9 do not recite a complete ion channel. Claims 1 and 19 have been amended to recite a "functional ion channel having an external vestibule." Descriptive support for this amendment is found in the specification at page 7, lines 22-23 and lines 27-28, page 8, lines 2-3, and page 17, line 25. Claim 1 has also been amended to recite that ion channel blockers are identified as such by their ability to "inhibit[] ion transport through the ion channel by binding to the external vestibule portion of the ion channel." Descriptive support for this amendment is found in the specification at page 8, lines 3-6, 15-18, and 20-24. In addition, the Huang Declaration demonstrates that experimental data has shown that the binding of a blocking agent (e.g., an antibody) to the external vestibule portion of the ion channel results in the inactivation of the ion channel (Huang Declaration ¶ 7). For example, experimental tests have shown that the antibody blocking effect of an ion channel's functionality could be attenuated by preincubating the antibody with an immunogenic peptide, but not with a control peptide (Id.). See Zhou et al., "Specific Antibodies to the External Vestibule of Voltage-Gated Potassium Channels Block Current," J. Gen. Physiol. 111:555-563 (1998) ("Zhou") (attached to the Huang Declaration as **Exhibit 6**). The data presented in Zhou demonstrates that the inhibition of the ion channel's activity is due to specific binding of an antibody to a particular peptide sequence located in the external vestibule (Huang Declaration ¶ 7).

Since the claimed invention is enabled by the present application, the rejection under 35 U.S.C. § 112 (1st para.) should be withdrawn.

In view of all of the foregoing, applicant submits that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

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Andrew K. Gonsalves
Registration No. 48,145

NIXON PEABODY LLP
Clinton Square, P.O. Box 31051
Rochester, New York 14603-1051
Telephone: (585) 263-1658
Facsimile: (585) 263-1600

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February 27, 2003 — Jo Ann Whalen
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Appendix A
Version With Markings to Show Changes Made
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In reference to the amendments made herein to claims 1 and 19, additions appear as underlined text, while deletions appear as bracketed text, as indicated below:

In the Claims:

1. (Four Times Amended) A method of identifying an ion channel blocker for an ion channel comprising:

providing a functional ion channel having an external vestibule portion [of an ion channel], wherein said external vestibule portion is the portion of the ion channel located between [the] an S5 transmembrane and pore forming region of the ion channel or between the pore forming region and [the] an S6 transmembrane of the ion channel, and

identifying, as an ion channel blocker for an ion channel, an antibody, binding portion of the antibody, probe, or ligand which inhibits ion transport through the ion channel by binding to the external vestibule portion of the ion channel [antibody, binding portion of the antibody, probe, or ligand binds to the external vestibule portion of the ion channel and is effective to inhibit ion transport through the ion channel].

19. (Thrice Amended) A method of screening a drug for effectiveness as an ion channel blocker for an ion channel, [wherein the ion channel has an external vestibule portion, said external vestibule portion being the portion of the ion channel located between the S5 transmembrane and pore forming region of the ion channel or between the pore forming region and the S6 transmembrane of the ion channel,] said method comprising:

contacting a cell, which cell has a functional ion channel having an external vestibule portion, [having an ion channel] with a drug which is an ion channel blocker candidate, wherein the external vestibule portion is a portion of the ion channel located between an S5 transmembrane and pore forming region of the ion channel or between the pore forming region and an S6 transmembrane of the ion channel;

evaluating the cell to determine if the ion channel blocker candidate binds to the external vestibule portion of the ion channel and inhibits ion transport through the ion channel; and

identifying a drug which binds to the external vestibule portion of the ion channel and inhibits ion transport through the ion channel as an ion channel blocker.